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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,453	04/16/2001	Dan M. Granoff	CHIR-0283	1041

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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 02/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/701,453	GRANOFF ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-29* is/are pending in the application.

4a) Of the above claim(s) *29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicants' submission filed 12/20/04 has been entered.

Applicants' Amendment

2) Acknowledgment is made of Applicants' amendment filed 12/20/04 in response to the final Office Action mailed 12/03/03 and the Advisory Action mailed 07/19/04.

Status of Claims

3) Claims 17 and 23 have been amended via the amendment filed 12/20/04.

Claims 17-29 are pending.

Claims 17-28 are under examination.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Withdrawn

6) The rejection of claims 17-23 and 25 made in paragraph 11 of the Office Action mailed 12/03/03 and maintained in paragraph 14 of the Office Action 07/19/04 under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698,1992 - already of record) and van der Voort *et al.* (*Infect. Immun.* 64: 2745-2751, 1996) in view of Paradiso *et al.* (*Dev. Biol. Stand.* 87: 269-275, 1996 - already of record), is withdrawn. A modified rejection is set forth below to meet the claims and/or the base claim as amended.

7) The rejection of 24 made in made in paragraph 12 of the Office Action mailed 12/03/03 and maintained in paragraph 15 of the Office Action 07/19/04 under 35 U.S.C § 103(a) as being

unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698,1992 - already of record) and van der Voort *et al.* (*Infect. Immun.* 64: 2745-2751, 1996 - already of record) in view of Paradiso *et al.* (*Dev. Biol. Stand.* 87: 269-275, 1996 - already of record) as applied to claim 17 above, and further in view of Granoff (US 6,413,520, already of record), is withdrawn. A modified rejection is set forth below to meet the base claim as amended.

Rejection(s) under 35 U.S.C § 112, First Paragraph (New Matter)

8) Claim 17 and those dependent therefrom are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The base claim 17 now includes the generic limitation: 'and an adjuvant'. Applicants point to page 2, line 30 to page 3, line 1; page 7, lines 20-21; and page 9, line 25 of the specification as providing descriptive support for these limitations. While there is descriptive support in these portions of the specification for a vaccine composition comprising a combination of NIPH NmB vaccine and the Chiron NmC conjugate vaccine in combination with the specific adjuvant species, MF59 or alum, there appears to be no support for a composition comprising any generic 'adjuvant' other than MF59 or alum. The scope of the generic term 'adjuvant' is not the same as the scope of the specific term 'MF59' or 'alum'. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to remove the new matter from the claim(s), or invited to point to specific pages and line numbers in the originally filed specification where support for such a recitation can be found.

Rejection(s) under 35 U.S.C § 103

9) Claims 17-23 and 25-27 are rejected under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698,1992 - already of record) and van der Voort *et al.* (*Infect. Immun.* 64: 2745-2751, 1996 - already of record) in view of Paradiso *et al.* (*Dev. Biol. Stand.* 87: 269-275, 1996 - already of record).

Costantino *et al.* taught a conjugate vaccine comprising immunologically effective amounts of group C meningococcal oligosaccharides having a polymerization degree (DP) of up to 10 (i.e., about 12 repeating units) conjugated to CRM 197 and aluminium hydroxide adjuvant, and a method of inducing an immune response to group C *Neisseria meningitidis* by administering an immunologically effective amount of the vaccine to a subject (see page 693).

Costantino *et al.* do not teach the use of outer membrane vesicles from any strain, or from strain 44/76 of group B *Neisseria meningitidis* along with their conjugate vaccine.

However, van der Voort *et al.* disclosed an immunogenic group B meningococcal hexavalent outer membrane vesicle vaccine from the group B meningococcal reference strain H44/76, which induced increased levels of bactericidal antibodies as well as a method of immunizing a mammal with the vaccine. The hexavalent vaccine advantageously covers more than 80% of the group B meningococcal subtypes isolated in many countries (see abstract; page 2745;. Materials and Methods; Results; and Discussion).

Paradiso *et al.* taught that they have prepared immunogenic glycoconjugates of group C meningococcal saccharides covalently linked to the carrier CRM_{197} which elicited a booster response characteristic of a T-dependent response in humans. Paradiso *et al.* further taught that since group B meningococcal capsule is not very immunogenic in people, the alternative approach of using outer membrane vesicles from a virulent group B meningococcal strain has been sought (see page 272). Paradiso *et al.* expressly taught that outer membrane vesicles prepared from group B meningococcal strains contain an array of proteins and lipids, and that in future, it will be desirable to mix them with a vaccine comprising group C meningococcal conjugate to create a new set of formulation (see paragraph bridging pages 272 and 273). The full passage bridging pages 272 and 273 of Paradiso *et al.* is provided below, with the relevant salient portion highlighted by italicization (see paragraph bridging pages 272 and 273):

> A significant portion of the morbidity from meningococcus is caused by group B. Unfortunately, the capsule from group B is not very immunogenic in people because of the similarity to saccharide structures on human cells. For this reason, and because of the potential for anti-group B antibody to cross-react with brain tissue, alternative approaches have been sought. *Most of the work has been done on outer membrane vesicles prepared from cells of virulent group B strains [10]. It seem likely that in the future it will be desirable to mix such a vaccine with the group C and/or group A conjugates.* Since these vesicle preparations contain an array of proteins and lipids, the combinations will create a new set of formulation challenges not unlike those encountered in mixing conjugate vaccines with DTP. [Emphasis added].

The key teaching or suggestion relevant to the instant rejection expressly taught by Paradiso *et al.* is re-cited below with the motivational teaching highlighted by italicization:

> Most of the work has been done on *outer membrane vesicles* prepared from cells of virulent group B strains [10]. It seem likely that *in the future it will be desirable to mix such a vaccine with the group C and/or group A conjugates.* [Emphasis added].

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine van der Voort's immunogenic group B meningococcal hexavalent outer membrane vesicle vaccine from the group B meningococcal reference strain H44/76 with Costantino's group C *Neisseria meningitidis* oligosaccharide-CRM_{197} conjugate vaccine comprising the adjuvant to produce the instant invention, with a reasonable expectation of success, because Paradiso *et al.* expressly taught that it is desirable to mix a group C meningococcal conjugate with outer membrane vesicles prepared from group B meningococcal strains containing an array of proteins and lipids to create a new set of formulation. Since one of skill in the art would readily understand that Costantino's group C meningococcal oligosaccharide-containing vaccine would not induce immunity against group B meningococci, a major causative agent of meningitis, a skilled artisan would have been motivated to produce the instant invention for the expected benefit of not only eliciting antibodies against serogroup C meningococci, but also for eliciting advantageously bactericidal antibodies to, or for covering more than 80% of the group B meningococcal subtypes isolated in many countries as taught by van der Voort *et al.* With the Costantino's group A and/or C glycoconjugate comprising an adjuvant and van der Voort's group B meningococcal OMV known and available in the art, and given the express teaching or suggestion by Paradiso *et al.* that 'in the future it will be desirable to mix such a vaccine', i.e., outer membrane vesicles prepared from cells of virulent group B strains, with the group C and/or group A conjugates, one of skill in the art would have readily understood the desirability for 'mixing' Costantino's group C and/or group A glycoconjugate with van der Voort's group B meningococcal outer membrane vesicles.

Claims 22 and 26 are product-by-process claims which include the process limitation: 'vesicles are produced by a deoxycholate extraction process'. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the

> prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown that the underlying structure of the prior art group B meningococcal outer membrane vesicles differs from that of the instantly claimed vesicles.

Claims 17-23 and 25-27 are *prima facie* obvious over the prior art of record.

10) Claims 24 and 28 are rejected under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698,1992 - already of record) as modified by van der Voort *et al.* (*Infect. Immun.* 64: 2745-2751, 1996 - already of record) and Paradiso *et al.* (*Dev. Biol. Stand.* 87: 269-275, 1996 - already of record) as applied to claim 17 or 26 above, and further in view of Granoff (US 6,413,520, already of record) ('520).

The reference of Granoff ('520) is used in this rejection because it qualifies as prior art under 35 U.S.C § 102(e) and therefore is not disqualified as prior art under 35 U.S.C § 103(a).

The teachings of Costantino *et al.* as modified by van der Voort *et al.* and Paradiso *et al.* are explained above, which do not teach their composition to be further comprising polylactic acids and/or polyglycolic acids.

However, the use of polylactic acids and/or polyglycolic acids in combination with a meningococcal oligosaccharide conjugate was well known in the art at the time of the instant invention. For instance, Granoff ('520) taught combining carriers, such as, polylactic and polyglycolic acids with meningococcal glycoconjugates for the purpose of primary vaccination wherein carriers do not themselves induce the production of harmful antibodies (see lines 1-10 in column 6).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add Granoff's ('520) polylactic or polyglycolic acid to Costantino's composition as modified by van der Voort *et al.* and Paradiso *et al.* to produce the instant invention, with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing Costantino's composition as modified by van der Voort *et al.* and Paradiso *et al.* for primary vaccination without

inducing the production of harmful antibodies as taught by Granoff ('520).

Claims 24 and 28 are *prima facie* obvious over the prior art of record.

Remarks

11) Claims 17-28 stand rejected.

12) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Fax number for submission of amendments, responses or papers is (571) 273-8300.

13) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

14) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

February, 2005

S. DEVI, PH.D.
PRIMARY EXAMINER